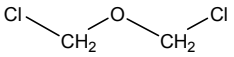
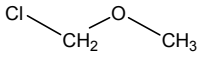
BIS(CHLOROMETHYL) ETHER AND TECHNICAL-GRADE CHLOROMETHYL METHYL ETHER

CAS Nos. 542-88-1 and 107-30-2

First Listed in the *First Annual Report on Carcinogens*



bis(Chloromethyl) ether



Chloromethyl methyl ether

CARCINOGENICITY

bis(Chloromethyl) ether and technical-grade chloromethyl methyl ether are *known to be human carcinogens* based on sufficient evidence of carcinogenicity in humans (IARC S.4, 1982; IARC S.7, 1987). Numerous epidemiological studies and case reports from around the world have demonstrated that workers exposed to chloromethyl methyl ether and/or bis(chloromethyl) ether have an increased risk for lung cancer. Among heavily exposed workers, the relative risks are tenfold or more. Risks increase with duration and cumulative exposure. Histological evaluation indicates that exposure results primarily in lung cancer of the small-cell type. Maximal relative risks appear to occur 15 to 20 years after first exposure, and latency is shortened among workers with heavier exposure.

An IARC Working Group reported that there is sufficient evidence of carcinogenicity of bis(chloromethyl) ether and technical-grade chloromethyl methyl in experimental animals (IARC V.4, 1974; IARC S.1, 1979; IARC S.4, 1982; IARC S.7, 1987). The evaluation of technical-grade chloromethyl methyl ether alone is complicated by the presence of 1 to 8% bis(chloromethyl) ether as a contaminant. Technical-grade chloromethyl methyl ether produced local sarcomas in mice after its subcutaneous administration and was an initiator of mouse skin tumors after topical application. It produced a low incidence of tumors of the respiratory tract in rats and hamsters after exposure by inhalation. When administered by subcutaneous injection, bis(chloromethyl) ether induced pulmonary tumors and local fibrosarcomas in mice of both sexes and fibromas and fibrosarcomas in female rats. The compound is also an initiator of skin tumors in mice. When administered by inhalation, bis(chloromethyl) ether induced lung tumors in mice and squamous cell carcinomas of the lung and esthesioneuroepitheliomas of the nasal cavity in rats. When applied topically, bis(chloromethyl) ether induced papillomas, most of which progressed to squamous cell carcinomas, in female mice (IARC S.1, 1979; IARC V.4, 1974).

PROPERTIES

bis(Chloromethyl) ether and chloromethyl methyl ether are water-soluble, colorless liquids. The former has a suffocating odor, while the latter has an irritating odor. Their decomposition in air is less rapid than in water. In moist air, bis(chloromethyl) ether decomposes into hydrogen chloride and formaldehyde. bis(Chloromethyl) ether can form whenever formaldehyde, water, and hydrogen chloride vapors are mixed at room temperature, even in low concentrations. When heated to decomposition, these chemicals emit toxic fumes of hydrochloric acid and other chlorinated compounds.

USE

bis(Chloromethyl) ether and chloromethyl methyl ether are industrial chemicals used primarily in the synthesis of plastics and ion-exchange resins (HSDB, 1997). bis(Chloromethyl) ether was once used for crosslinking of cellulose, surface treatment of vulcanized rubber to increase adhesion, and in the manufacture of flame-retardant fabrics (ATSDR, 1989-K009). Today, it is used mainly as a chemical intermediate and has potential use in dental restorative materials. Furthermore, bis(chloromethyl) ether is used as the monitoring indicator for chloromethyl methyl ether because of its greater stability in workroom air (HSDB, 1997).

PRODUCTION

Chem Sources identified 8 distributors of chloromethyl methyl ether and two high purity distributors among the five listed for bis(chloromethyl) ether (Chem Sources, 1991). The USITC has identified one domestic producer of chloromethyl methyl ether since 1987, but no production data have been reported (USITC, 1988-1991, 1993-1994). The 1979 TSCA Inventory identified four domestic producers of chloromethyl methyl ether, with a total of 31 million lb produced in 1977 with some site limitations, and one producer of bis(chloromethyl) ether with a volume of 550,000 lb, also with some site limitations. The CBI Aggregate was between 100 million and 1 billion lb for both chemicals (TSCA, 1979). Although significant quantities of bis(chloromethyl) ether were previously manufactured in this country, use of this chemical and other chloromethyl ethers was curtailed in 1976 (HSDB, 1997), following stringent regulation by the Occupational Safety and Health Administration. Available information indicates that bis(chloromethyl) ether is no longer produced as a commercial product in the United States (ATSDR, 1989-K009; HSDB, 1997). Despite this, it is possible that small quantities occasionally may be produced and used in captive processes within chemical factories. bis(Chloromethyl) ether is produced as a contaminant during the manufacture of chloromethyl methyl ether, usually at levels of 0.5 to 5% (ATSDR, 1989-K009). Technical grades of chloromethyl methyl ether are contaminated with 1 to 8% bis(chloromethyl) ether (IARC V.4, 1974). No data on imports or exports were available for these compounds.

EXPOSURE

The primary routes of potential human exposure to bis(chloromethyl) ether and technical-grade chloromethyl methyl ether are inhalation and dermal contact. Because bis(chloromethyl) ether is used very little in this country and because it is rapidly degraded in the environment the probability of human exposure to bis(chloromethyl) ether is very low—close to zero; it has not been detected in ambient air or water (ATSDR, 1989-K009). The Toxic Chemical Release Inventory (EPA) listed two industrial facilities that produced, processed, or otherwise used bis(chloromethyl) ether in 1988 and four for chloromethyl methyl ether (TRI, 1990). In compliance with the Community Right-to-Know Program, the facilities reported releases of bis(chloromethyl) ether to the environment, which were estimated to total one lb, and the releases of chloromethyl methyl ether, which were estimated to total 120 lb. Very low incidental exposure may also occur because of metabolites of some dental materials regulated by FDA.

Occupational exposure to chloromethyl methyl ether is minimized since most industrial operations working with the chemical are carried out in closed process vessels. The most likely means of exposure to bis(chloromethyl) ether is inhalation of its vapors in the workplace during the production and use of chemicals in which bis(chloromethyl) ether may occur as a

contaminant or may be formed inadvertently (ATSDR, 1989-K009). The risk of potential occupational exposure to the chemicals is greatest for workers such as chemical plant workers, ion-exchange resin makers, laboratory workers, and polymer makers. The National Occupational Exposure Survey (1981-1983) indicated that 14 workers, including 5 women, were potentially exposed to bis(chloromethyl) ether (NIOSH, 1984). This estimate was based only on observations of the actual use of the compound. ACGIH has assigned a TLV of 0.001 ppm for bis(chloromethyl) ether; no TLV has been assigned for chloromethyl methyl ether (ACGIH, 1986). Residents near a facility or waste site may be exposed to escaped bis(chloromethyl) ether, but there are no data indicating whether this occurs or not or if it should be of concern (ATSDR, 1989-K009).

REGULATIONS

A preliminary determination by CPSC in 1980 indicated that these chemicals were not present in consumer products under CPSC jurisdiction. CPSC subsequently requested public comment to verify the accuracy of its information, and no comments were received on the chemicals. Pending the receipt of new information, CPSC plans no action on these chemicals. EPA regulates bis(chloromethyl) ether and chloromethyl methyl ether under the Clean Water Act (CWA), Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), Resource Conservation and Recovery Act (RCRA), Superfund Amendments and Reauthorization Act (SARA), and Toxic Substances Control Act (TSCA). Reportable quantities (RQs) of 10 lb have been established for both compounds under CERCLA. They are considered hazardous constituents of waste regulated under RCRA, and listed as extremely hazardous substances under EPCRA. bis(Chloromethyl) ether, however, was deleted from the hazardous substance list of the CWA because of its extremely short half-life in water and the absence of data indicating it is a water pollution problem. Both compounds are subject to reporting under SARA. The possible presence of bis(chloromethyl) ether in dental restorative materials is noted by the FDA; exposure is considered incidental. NIOSH (1994) has recommended that exposure to bis(chloromethyl) ether and chloromethyl methyl ether be limited to the lowest feasible concentration. OSHA issued an emergency temporary standard covering both chemicals in 1973, and a final standard in 1974; this standard prohibits operations in open vessels and requires exhaust fans, protective clothing and devices, and warning signs and labels. OSHA also regulates occupational exposure to bis(chloromethyl) ether and chloromethyl methyl ether as potential carcinogens. It further regulates the two as chemical hazards in laboratories under the Hazard Communication Standard. Regulations are summarized in Volume II, Table A-10.